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Organ-Preserving Management of Rhabdomyosarcoma of the Prostate and Bladder in Children

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Between November 1978 and July 1991, ten children between one and eight years of age with Group III pelvic rhabdomyosarcoma (IRS classification) and considered inoperable at diagnosis were treated primarily with intensive poly-chemotherapy. Complementary radiotherapy and conservative surgery were added as needed. Eight of the ten survive free of disease with functioning bladders for periods ranging from 5.7–18.4 years. Med. Pediatr. Oncol. 29:573–575, 1997.

Key words: pediatric oncology; soft tissue sarcoma; genito-urinary cancer

INTRODUCTION

Rhabdomyosarcoma (RMS) is the most common sarcoma of soft tissues affecting children and adolescents [1,2]. Before 1950, pelvic origin mandated radical surgery and/or radiotherapy with almost always disappointing results. Then, encouraging tumor responses to chemotherapy became a matter of record after treatment with vincristine and dactinomycin. This allowed the role of surgery to be reassessed, and multiple agent chemotherapy trials were initiated [3–5]. These have made possible studies to avoid extensive procedures, limiting surgery to the taking of biopsies and to the removal of residual masses [6–9].

This approach was used in the management of 10 children with Stage III pelvic RMS seen at the ''Virgen del Rocio'' University Children's Hospital in Seville.

MATERIALS AND METHODS

A total of 63 patients with RMS were seen at our hospital in the period November 1978 to July 1991. Of the 63 children, ten had pelvic primary neoplasms. Their ages ranged from 1.5–8 years; 8 were males (Table I). Biopsies were obtained in all ten using the following techniques: 4: transurethral biopsy, 4: needle biopsy with Tru-cut needle**, 2: exploratory laparotomy with biopsy. All the tumors were of the embryonal type, 5 of them being botryoid.

The size, location, and stage of the tumors were established by CAT scans, magnetic resonance imaging, urography, cystoscopy, chest x-ray films, bone scans, and bone marrow aspirate and biopsy. The tumor was in the bladder in 5 patients, vesico-prostatic in 4 patients and prostate alone in one. They were all considered Group III of the Intergroup Rhabdomyosarcoma Study because they had only a biopsy before therapy was instituted, and none had metastases at diagnosis [2].

Surgical management was considered inappropriate because it would have involved exenterations of the anterior pelvic contents in all ten children. All patients therefore received intensive chemotherapy (Table I). The first three patients were treated according to the so-called T-2 protocol of the Memorial Sloan-Kettering Cancer Center (MSKCC) for induction and maintenance [4]. It includes dactinomycin, vincristine, doxorubicin, and cyclophosphamide. The seven later patients received the two induction cycles of the T-6 MSKCC protocol in which higher doses of the four agents previously mentioned are used plus bleomycin and methotrexate [5]. This was followed by maintenance with 4 cycles of a modified T-6 regimen in six cases or the T-2 regimen in one case. Radiation therapy was given to nine of the

**Urinary cytology also was positive in one of the patients diagnosed by needle biopsy.

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TABLE I.

Pt #	Age at Dx (yrs)	Sex	Stage	Primary site	Type of surgery	Radio-therapy (Gy)	Chemo-therapy	Status	Survival from Dx (mos)	Sites of metastasis or local recurrence
1.	4	M	III	Prostate	Bx	30	A	Dead	11	Local Relapse
2.	2–3/12	M	III	Bladder	TX & PND	42	A	NED	221	—
3.	6–5/12	M	III	Bladder	Bladder & node & Bx	40	A	NED	219	—
4.	7–7/12	M	III	Bladder	Bladder & node & Bx	40	B	NED	178	—
5.	3–5/12	M	III	Prostate Bladder	BX and PND	50	C	NED	164	—
6.	4–10/12	M	III	Prostate Bladder	Bx & Tx & PND	40	C	NED	146	—
7.	1–5/12	M	III	Prostate Bladder	Bx Cytology	51	C	NED	118	—
8.	8	M	III	Prostate Bladder	Bx	—	C	Dead	22	Lung
9.	1–5/12	F	III	Bladder	Tx & PND & retroperitoneal node dissection	50	C	NED	85	—
10.	1–8/12	F	III	Bladder	Bx	46.5	C	NED	68	—

Abbreviations: Bx = biopsy, PND = pelvic node dissection, Tx = tumorectomy; Chemotherapy used: A = T2 for induction and maintenance; B = T6 for induction and T2 for maintenance; C = T6 for induction and T6M for maintenance (see text).

children during the first two cycles of chemotherapy when total doses of between 30–51 Gy were delivered. Patients were then submitted to exploratory laparotomy 4–8 months after the initiation of chemotherapy.

RESULTS

Eight of the ten children are still alive relapse-free and with functioning bladders for periods ranging between 5.7 and 18.4 years (Table I). One patient died 11 months after diagnosis from progression of local disease. One developed pulmonary metastases 22 months after diagnosis and died shortly afterwards, free of pelvic recurrence.

Hemorrhagic cystitis was the most important of the complications encountered in the early years of this study before mesna protection was known [3]. Otherwise, the acute complications were those anticipated from multiagent chemotherapy. One of the children developed urethral stenosis four years after the initiation of chemotherapy and radiation therapy.

DISCUSSION

The previous dismal outlook for patients with pelvic rhabdomyosarcoma (RMS) has been altered by the advent of effective chemotherapy. This has encouraged attempts to avoid radical surgical extirpations of pelvic organs, surgery being limited to biopsies and partial resections of tumors remaining after combined chemo-radiation therapy. It is interesting to note that needle biopsy and/or aspirate in our hands were effective substitutes for conventional excisional biopsy. These examinations when reviewed by experienced cyto-pathologists avoid the need for open surgical biopsies at least in some patients.

Ortega et al. [6] reported success in two of three stage III children with pelvic RMS treated without exenteration. Ghavimi et al. reported 75% survival in 29 patients, but 12 of them needed exenteration because of failure of chemotherapy and radiation therapy to secure a complete response. Hays et al. [11,12] provided results of the Intergroup Rhabdomyosarcoma Study (IRS). In the first IRS I (1972–78), total cystectomy was the initial surgical procedure in most primary patients with pelvic RMS. In IRS II (1979–1984) primary chemotherapy, pulse VAC*/28 and with transfer to pulse VadrC* plus 25–45 Gy radiation therapy (RT) was employed in an attempt to avoid total exenteration or cystectomy. Despite these differences in approach, results in IRS I and II were similar, with a mortality of 26–30% and a rate of retained functional bladders among survivors of 22–25% at three years. In IRS III (1985–1990) primary chemotherapy was intensified and also RT to 45 Gy in 5–6 weeks. Delayed partial cystectomy or prostatectomy was performed in some patients. The overall survival in this group at three years is 90% (73/81) vs. 70% in IRS II, and there has been no bladder loss after 18 months on therapy.

Verga et al. [13] and Hicks et al. [14] recently de-

*VAC = vincristine, dactinomycin, cyclophosphamide. VadrC = vincristine, doxorubicin, cyclophosphamide.

scribed their management of patients with pelvic RMS. Seven of ten were treated conservatively by Verga et al. and six survived disease-free with a normal, functional bladder after 10–21 years. All three of their patients who underwent radical surgery, died. By contrast Hicks and colleagues used more radical surgery. Six of their 14 patients had exenterative procedures and all 14 patients survived.

It is difficult to compare the regimens employed by us with those of the many other reports because those authors fail to provide specifics regarding the multi-modal and multi-agent chemotherapy they used. Others report only overall survival rates without giving relapse-free percentages. Nonetheless, our results with preservation of the bladder, compare favorably with those reviewed above and with the report by Heij et al. from The Netherlands [15]. The Amsterdam group, which has been a pioneer in exploring methods of preserving the pelvic organs, makes the extremely important point that very long and careful follow-up is needed in patients in whom local control appears to have been successful. One of their patients, a boy who underwent an exenterative operation, relapsed locally 8.5 years after diagnosis. Six out of eight of our patients have survived with functioning bladders beyond that point (for 9.8–18.4 years); our other two survivors are under continuing surveillance for periods of 68 and 85 months respectively.

CONCLUSION

We conclude that aggressive chemotherapy regimens* with frequent surveillance and exploratory laparotomies as used by us have so far been successful in preserving the bladders of our eight patients who survive for 5.7–18.4 years.

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*The T2 and T6 regimens used by us have since been replaced by other drug combinations and are not to be taken as the treatments of choice.

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